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In vitro sodium salicylate release from chitosan films

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SUMMARY

In order to evaluate the applicability of chitosan membranes in controlled release systems, a reservoir-type device was designed. Sodium salicylate was chosen as model drug. The rate of release was measured in water at 37Ω ± 0.5Ω C and the amount of drug released was determined by spectrophotometric analysis. The results showed that sodium salicylate release followed a zero order kinetics.

INTRODUCTION

Chitosan is a polyaminosaccharide obtained by alkaline N-deacetylation of chitin which is widely distributed in nature. Both chitin and chitosan are biodegradable, biocompatible and have low toxicity (1,2). These properties turn chitosan into a suitable carrier of pharmaceutical agents in controlled delivery systams. Several examples have been reported about chitin and chitosan gels as carriers of indomethacin, papaverine hydrochlorida (3,4) and cisplatin (5,6).

Among all the new controlled release technologies, the use of membranes is the most promising due to their ability to maintain constancy in the drug delivery profiles. M. Kanke and co-workers have used chitosan membranes containing prednisolone as model drug dispersed on the polymeric matrix (7).

In the present work, chitosan membrane was used in an in vitro study about controlled release employing sodium salicylate as model drug.

EXPERIMENTAL

Chemicals and Reagents: Chitosan was a commercial sample from Crab Shells (practical grade) purchased from Sigma. Chitosan was purified as follows: it was dissolved in 1 M aqueous acetic acid, filtered and reprecipitated by addition of 3.6 N sodium hydroxide, then repeatedly washed with distilled water up to pH = 7. The N-acetyl content was determined by first derivative ultraviolet spectrophotometry (8) and was found in around 14.5 %. The viscosity-average molecular weight (9,10) was 5.90×10^5. Sodium salicylate of analytical grade

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was used without further purification.

Apparatus: The spectrophotometric studies were carried out on a Shimadzu UV 260 spectrophotometer. A constant-temperature bath which was regulated by a Haake E2 thermostat with ± 0.5 ºC precision was used.

Preparation of chitosan films: The chitosan solution was prepared at 1% w/v in 1M acetic acid, filtered and poured into a Petri dish. It was then kept at 60º C until complete evaporation of the solvent. The membrane obtained was left for 24 h in 1M NaOH aqueous solution at room temperature and then repeatedly washed with distilled water. The thickness of the membrane swollen in water was determined with an optical microscope.

Measurement of water content (W) of the membrane: A weighed sample of the membrane, without drug, was immersed in deionized water and swollen in a vessel thermostated at 37 ºC. The swollen sample was removed from the water at regular time intervals and the excess solution on the swollen sample was absorbed by gentle tamping between filter papers. The sample was weighed and the procedure was repeated until a constant weight was achieved. Measurements were performed in triplicate. The swelling degree was calculated from the following equation (11):

$$(W) = 100\left(\frac{\text{weight of swollen sample} - \text{weight of dry sample}}{\text{weight of swollen sample}}\right)$$

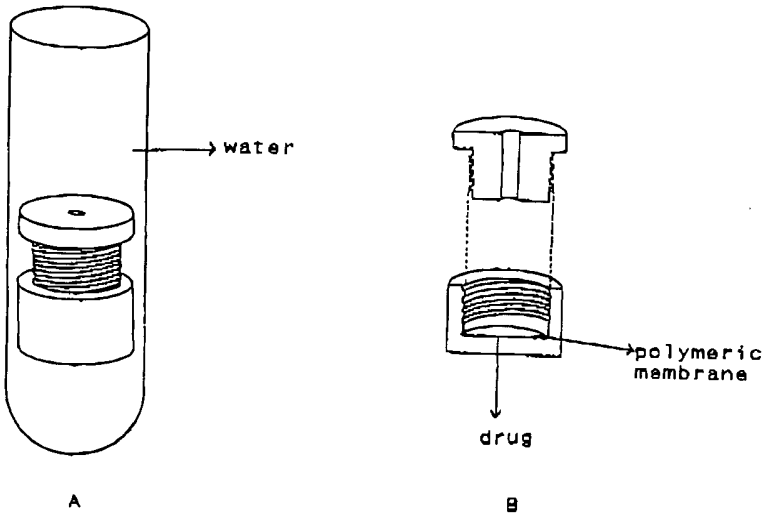
Apparatus for measurement: The reservoir-type device (12) consisted of a glass tube and a stoppered Teflon vessel that had a 3 mm diameter hole on the upper face. The solid drug which was covered by the chitosan membrane swollen in water is placed at the bottom of the stoppered vessel.

Measurement of the amount of the drug released: Water (30 ml) was used in the extractions. Drug release experiments were carried out in a thermostated bath at 37º C with continuous stirring. The amount of released drug was spectrophotometrically determined. The samples were taken at regular time intervals and the extractant was renewed after each measurement. The studies were made in triplicate and the average values were plotted.

RESULTS AND DISCUSSION

The diffusion studies were carried out using a reservoir-type device (Fig. 1) under the following constant conditions: container of saturated drug, continuous stirring and periodic renewal of the release medium.

A chitosan membrane, prepared by solvent evaporation, with a total water content at equilibrium of 50.7 % was used. The thickness of the water swollen membrane was 304 µ. Sodium salycilate was chosen as model drug owing to its solubility in water and suitable UV absorption (Table 1).



A - Device placed inside the glass tube.
B - Longitudinal cut of the device.

Figure 1: Apparatus for measurement.

Figure 2 shows the amount of drug released as a function of time. The average values are plotted in the figure. The reproducibility in triplicate runs was good. A nonlinear time lag can be observed, that is, the time it takes the drug to cross the membrane and begin to release, followed by a linear range with a correlation coefficient of 0.986. The parameters for the linear range were calculated by linear regression. The release rate of sodium salicylate in water was 7.4 $x10^{-2}$ mg/min. Zero order kinetics is most desirable in controlled release systems.

These preliminary studies suggest that chitosan membranes can be employed as controlled-release devices for pharmaceutical agents using a reservoir-type device.

Table 1: Molecular Weight, Water Solubility, Analytical Wavelength and Molar Absorptivity Coefficients of Sodium Salicylate.

Drug	Mol.wt.	Cs (mg/ml)	λ_{max}	ε (l/mol.cm)
Sodium Salicylate	160.11	1111	294.0	3620

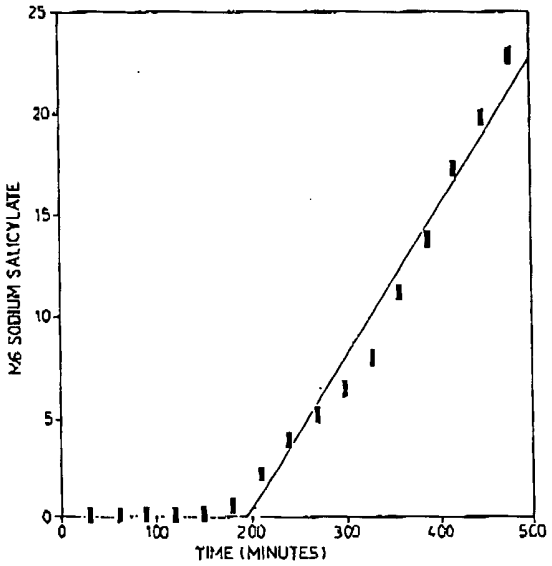


Figure 2: Sodium salicylate release from chitosan membranes.

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